## Bovine pericardial extracellular matrix niche modulates human aortic endothelial cell phenotype and function.

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**Public Summary:**
Bovine pericardium is used as a tissue engieered scaffold for surgical grafting. Bovine pericardium has to distinct sides with different tissue properties (for example, basement membrane, also known as serous side vs. non-basement membrane, also known as fibrous side). We have tested the effect of this different tissue architecture of antigen-removed bovine pericardium (AR-BP, deplited of cell content) on human aortic endothelial cells (hAEC) repopulation. We seeded hAEC on both sides of the AR-BP and tested cell adhesion, growth, phenotype, inflammatory response and laminin production. At low and moderate seeding densities, hAEC proliferation was significantly increased on the serous side. Similarly, cellular morphology was distinc in both sides, with serous side seeding resulting in more rounded cells and intact endothelial layer formation. At moderate seeding densities, hAEC production of human laminin was enhanced following serous seeding. Finally, inflammatory marker and pro-inflammatory cytokine expression decreased following long-term cell growth regardless of seeding side. This work demonstrates that at low and moderate seeding densities AR-BP sidedness significantly impacts endothelial cell growth, morphology, human laminin production, and inflammatory state. These findings suggest that tissue conformation has a role in modulating response of repopulating newly seeded cells toward AR-BP scaffolds for vascular applications.

**Scientific Abstract:**
Xenogeneic biomaterials contain biologically relevant extracellular matrix (ECM) composition and organization, making them potentially ideal surgical grafts and tissue engineering scaffolds. Defining the effect of ECM niche (e.g., basement membrane vs. non-basement membrane) on repopulating cell phenotype and function has important implications for use of xenogeneic biomaterials, particularly in vascular applications. We aim to understand how serous (i.e., basement membrane) versus fibrous (i.e., non-basement membrane) ECM niche of antigen-removed bovine pericardium (AR-BP) scaffolds influence human aortic endothelial cell (hAEC) adhesion, growth, phenotype, inflammatory response and laminin production. At low and moderate seeding densities hAEC proliferation was significantly increased on the serous side. Similarly, ECM niche modulated cellular morphology, with serous side seeding resulting in a more rounded aspect ratio and intact endothelial layer formation. At moderate seeding densities, hAEC production of human laminin was enhanced following serous seeding. Finally, inflammatory marker and pro-inflammatory cytokine expression decreased following long-term cell growth regardless of seeding side. This work demonstrates that at low and moderate seeding densities AR-BP sidedness significantly impacts endothelial cell growth, morphology, human laminin production, and inflammatory state. These findings suggest that ECM niche has a role in modulating response of repopulating recipient cells toward AR-BP scaffolds for vascular applications.